REMARKS / ARGUMENTS

Claims 1, 3-10, 17, 19, 23-25, and 26-27 remain in this application. Claims 2, 18, 20-22 have been canceled without prejudice to prosecuting these same, or similar claims, in subsequently filed applications. Claims 11-16 have been withdrawn without prejudice to prosecuting these same, or similar claims, in subsequently filed applications. Claims 26 and 27 are "new" claims introduced in the instant correspondence.

Claims 1, 3-10, 17, 19, 23-25 were rejected. The Examiner made the following rejections:

(1) Claims 1, 3-10, 17, and 23-25 were rejected under 35 U.S.C. 112 (second paragraph).

Applicants believe the following remarks, and the attached declaration of Dr. James R. Connor, traverse the Examiner's rejection of the claims.

1. The Claims Are Definite

In previous correspondence, the Applicants have: i) cited to well settled law supporting the proposition that claims of a patent application *are to be construed in the light of the specification* and ii) pointed to multiple sections, in the application as filed, that teach how *any* difference in the degree of binding of an iron binding protein, between an experimental and control brain tissue sample, confirms the detection of multiple sclerosis in said experimental brain tissue sample. Notwithstanding this showing by the Applicants, the Examiner continues to reject claims 1, 3-10, 17 and 23-25 under 35 U.S.C. 112, second paragraph.

The Examiner is reminded that the first sentence of 35 U.S.C. § 112 (second paragraph) is essentially a requirement for precision and definiteness of claim language. Whether a claim is invalid for indefiniteness, however, depends on whether those skilled in the art would understand the scope of the claim when the claim is read in light of the specification. See, *North American Vaccine, Inc. v. American Cyanamid Co.*, 28 USPQ 2d 1333, 1339 (Fed. Cir. 1993). An Examiner's *opinion* as to what a skilled artisan would /

would not know in view of the teaching provided by the Applicants is not sufficient to support a rejection. The Applicants respectfully note that the Examiner is not considered (under the law) "one of skill in the art." See, *Stratoflex, Inc. v. Aroquip Corp.*, 218 USPQ 871, 879 (Fed. Cir. 1983).

Moreover, "if the rejection is based on facts within the personal knowledge of the examiner, the data should be stated as specifically as possible, *and the facts must be supported when called for by the applicant, by an affidavit from the examiner.*" MPEP 2144.03 (emphasis added). The Examiner provides no such affidavit. In contrast, however, Applicants offer (under 37 C.F.R. § 1.132) the fact based declaration of Dr. James R. Connor in support of their rebuttal of the Examiner's rejection of the pending claims.

A. Potential Variations In Control Tissue Samples Do Not Compromise The Methods As Claimed

The Examiner states,

> "one skilled in the art would reasonably assume that any two brain tissue samples even from two normal unaffected individuals would display some differences in binding of iron binding protein, or, in other words, would not be completely identical in the pattern of binding distribution"[1]

As a threshold observation, the Applicants object to the Examiner suggestion that alleged variance in the binding of an iron binding protein between *control* human brain tissue samples, somehow, compromises ability to compare differences in the degree of binding of an iron binding protein to: i) a first brain tissue sample from a human suspected of having a demyelinating disease and ii) a second brain tissue sample from a human free from the pathological manifestations of a demyelinating disease. As noted in the attached Declaration of Dr. James R. Connor (herein after referred to as the "Connor Declaration"),

> "in terms of the claimed detection methods, no significant differences were seen in the distribution of iron binding proteins between (control) tissue obtained from different individuals (e.g. surgical patients vs. cadavers) free from the pathological manifestations of a demyelinating disease. Moreover, the fact that these control sample can be stored for up to two weeks, with no noticeable loss in binding activity, is evidence of the robustness of the detection methods as claimed." See, Connor Declaration, paragraph 3.

---

[1] Office Action mailed April 28, 2003, page 3.

In view of this statement by the Declarant, the Examiner's speculation that different control samples may "not be completely identical in the pattern of binding distribution" (*supra*) is of no moment. That is to say, the Declarant confirms that "no significant differences were seen in the distribution of iron binding proteins between (control) tissue obtained from different individuals" (*supra*).

Therefore, one of skill in the art has expressly rebutted the Examiner's contention that the control tissue, incorporated into some of the pending method claims, are subject to some alleged variance that would compromise the comparison, of the degree of binding of an iron binding protein, to an experimental tissue sample (from a human suspected of having a demyelinating disease) and a control brain tissue sample (from a human free from the pathological manifestations of a demyelinating disease).

B. Comparing Differences In Degrees Of Binding Is Definite

The claimed methods make use of distinct changes in the binding and localization of iron binding proteins in the brains tissue of a person having a demyelinating disease.[2] As noted in the Connor Declaration,

> "In one embodiment of the present invention, the decrease in ferritin binding (observed in CNS lesions and periplaque margins of an experimental brain tissue sample) is an indicia consistent with a finding of a demyelinating disease." Connor Declaration, paragraph 4.

and,

> "In one embodiment of the present invention, the binding of transferrin (in periplaque regions of an experimental brain tissue sample) is another indicia consistent with a finding of a demyelinating disease." Connor Declaration, paragraph 5.

---

[2] Applicants introduce, in the instant Preliminary Amendment, two new independent claims specific for a given iron protein (e.g. ferritin in claim 26 and transferrin in claim 27). Each of these claims uses the binding profile (in a brain tissue sample form a human suspected of having a demyelinating disease) unique to each of these iron binding proteins to confirm the detection of multiple sclerosis in a brain tissue sample. In this respect, the Applicants note that claims 26 and 27 do not incorporate the use of a control tissue sample.

That is to say, different iron binding proteins (e.g. ferritin and transferrin) bind differently to: i) brain tissue from a human suspected of having a demyelinating disease and ii) brain tissue from a human free of the pathological manifestations of a demyelinating disease. See, Connor Declaration, paragraph 6.

The Examiner states,

> "it is not clear what difference or degree of difference is indicative of multiple sclerosis. . .[t]he Examiner maintains the position that the last step of the claimed method is indefinite because terms 'degree' and 'difference" are relative terms and until a point of reference is clearly identified, a skilled artisan would not know what level of 'degree of binding' or 'difference in said binding' is indicative of multiple sclerosis."[3]

It should be noted this "difference" refers to the difference in binding of an iron binding protein to a first (i.e. experimental) brain tissue sample versus a second (i.e. control) brain tissue sample.

As noted in paragraphs 4 and 5 of the Connor Declaration, however, human brain tissue affected by demyelinating disease presents a *difference*, vis-a-vis normal brain tissue, in the binding and localization of iron binding proteins in these same tissues.

Moreover, as noted by Dr. Connor,

> "[a]s noted in the specification of the application as filed, different iron binding proteins bind differently to: i) brain tissue from a human suspected of having a demyelinating disease and ii) brain tissue from a human free of the pathological manifestations of a demyelinating disease."
> Connor Declaration, paragraph 6.

In this respect, and contrary to the Examiner's assertion, the second brain tissue sample (i.e. the control sample) does provide a point of reference from which a difference in degree of binding may be compared. That Furthermore, as noted by Dr. Connor:

> "[g]iven the discrete binding profiles of iron binding proteins to control and experimental tissue samples (as discussed in the paragraphs above), one of skill in the art would be able to evaluate the differences in the degree of binding of iron binding protein to, i) the first brain tissue sample (e.g. the experimental sample) and ii) the second brain tissue sample (e.g. the control) as part of a method for the detection of multiple sclerosis."
> Connor Declaration, paragraph 7.

---

[3] Office Action mailed April 28, 2003, page 3.

Applicants provide evidence that establishes: i) the *bona fides* of control tissue sample and ii) the ability of one of skill in the art to evaluate the differences in the degree of binding of iron binding protein to an experimental tissue sample and a control tissue sample as part of the claimed methods for the detection of multiple sclerosis. Therefore, in view of: i) the teaching provided by the application as filed and ii) the fact based declaration submitted by Dr. James R. Connor, Applicants respectfully submit their burden, under 35 U.S.C. §112(second paragraph), has been meet.

CONCLUSION

The Applicants believe the arguments set forth above traverse the Examiner's rejection and, therefore, request that the pending claims be passed to allowance. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, the Applicants encourage the Examiner to call the undersigned collect at 617.984.0616.

Dated: September 29, 2003

Thomas W. Brown
Registration No. 50,002

MEDLEN & CARROLL, LLP
101 Howard Street, Suite 350
San Francisco, California 94105
617.984.0616